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TOWNSEND and TOWNSEND and CREW LLP

By: MAIHAN VO

PATENT
Attorney Docket No.: 015270-006446US
Client Reference No.: 228-US-NEW2C6

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

John P. Anderson et al.

Application No.: 09/724,569

Filed: November 28, 2000

For: BETA-SECRETASE ENZYME
COMPOSITIONS AND METHODS

Examiner: Unknown

Art Unit: 1632

INFORMATION DISCLOSURE
STATEMENT UNDER 37 CFR §1.97 and
§1.98

Technology Center 1600
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The references cited on attached PTO/SB/08A and PTO/SB/08B forms are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 09/471,669, filed December 24, 1999 (Attorney Docket No. 015270-006430US). It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Cite no. 78 is a copy of the International Search Report issued for the corresponding International application, PCT/US00/03819. Cite No. 65 is a copy of a press release announcing that Elan Corporation, plc and Pharmacia Corporation entered into a research collaboration focused on the discovery of small molecule inhibitors of beta-secretase for the

treatment of Alzheimer's disease. Elan Pharmaceuticals, Inc. assignee of the instant application, is affiliated with Elan Corporation, plc.

Applicants also cite commonly owned copending applications and issued patents directed to related subject matter:

08/480,498, filed 06/07/95, issuing as US Patent 5,744,346 on April 28, 1998;
08/485,152, filed 06/07/95;
08/659,984, filed 06/07/96, issuing as US Patent 5,942,400 on August 24, 1999;
08/660,531, filed 06/07/96, issuing as US Patent 6,221,645 on April 24, 2001;
09/054,334, filed 04/02/98, issuing as US Patent 6,329,163 on December 11, 2001;
09/404,578, filed 09/23/99;
09/471,669, filed 12/24/99;
09/501,708, filed 02/10/00;
09/723,722, filed 11/28/00;
09/723,739, filed 11/28/00;
09/724,568, filed 11/28/00;
09/724,566, filed 11/28/00;
09/724,569, filed 11/28/00;
09/724,571, filed 11/28/00; and,
10/099,922, filed 03/15/02;

Applicants further cite the following commonly owned abandoned applications directed to related subject matter:

60/114,408, filed 12/31/98;
60/119,571, filed 02/10/99;
60/139,172, filed 06/15/99;
60/168,854, filed 12/02/99; and,
09/730,329, filed 12/04/00.

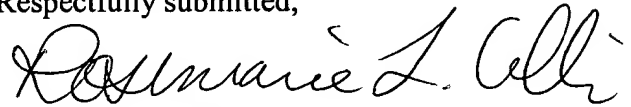
As provided for by 37 CFR 1.97(g) and (h), no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information, and no inference should be made that the information and references cited are, or are considered to be material to patentability because they are in this statement. No inference

should be made that the information and references cited are prior art merely because they are in this statement.

Applicant believes that no fee is required for submission of this statement.

However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Rosemarie L. Celli".

Rosemarie L. Celli
Reg. No. 42,397

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Sheet 1 of 6

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Application Number 09/724,569
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First Named Inventor John P. Anderson
Art Unit 1632
Examiner Name Unknown
Attorney Docket Number 015270-006446US

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U.S. PATENT DOCUMENTS

Examiner	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number Kind Code ² (if known)			
	1	6,361,975	03-26-2002	Christie, et al.	
	2	6,358,725	03-19-2002	Christie, et al.	
	3	6,319,489	11-20-2001	Powell, et al.	
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	5	6,313,268	11-06-2001	Hook	
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	8	6,221,645	04-24-2001	Chrysler, et al.	
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	17	5,766,846	06-16-1998	Schlossmacher, et al.	
	18	5,750,349	05-12-1998	Suzuki, et al.	
	19	5,744,346	04-28-1998	Chrysler, et al.	
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	23	5,424,205	06-13-1995	Dovey, et al.	
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	90	09/794,927		Gurney, et al.	
	91	09/794,925		Gurney, et al.	

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		Number Kind Code ² (if known)			
	89	09/795,847	NA	Gurney, et al.	
	92	09/794,748		Gurney, et al.	
	88	09/794,743		Gurney, et al.	
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	34	60/141,363		Lin, et al.	
	35	60/139,172		Anderson, et al.	
	36	60/119,571		Basi, et al.	
	37	60/114,408		Basi, et al.	
	38	60/101,594		Gurney, et al.	

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Attorney Docket Number	015270-006446US

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	39	EP	EP 0 855 444	A2	07-29-1998			
	40	EP	EP 0 848 062	A2	06-17-1998			
	48	PCT	WO 01/38487	A2	05-31-2001			
	49	PCT	WO 01/36600	A1	05-25-2001			
	50	PCT	WO 01/31054	A1	05-03-2001			
	51	PCT	WO 01/29563	A1	04-26-2001			
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	47	PCT	WO 00/69262	A1	11-23-2000			
	46	PCT	WO 00/68266	A1	11-16-2000			
	45	PCT	WO 00/58479	A1	10-05-2000			
	44	PCT	WO 00/56871	A2	09-28-2000			
	43	PCT	WO 00/47618	A3	08-17-2000			
	42	PCT	WO 00/23576	A2	04-27-2000			
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	62	PCT	WO 98/13488		04-02-1998			
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	58	PCT	WO 96/31122	A1	10-10-1996			
	102	PCT	WO 96/20725	A2	07-11-1996			
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First Named Inventor	John P. Anderson
Art Unit	1632
Examiner Name	Unknown
Attorney Docket Number	015270-006446US

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OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

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	104	Baldwin, et al., Crystal structures of native and inhibited forms of human cathepsin D: Implications for lysosomal targeting and drug design, <i>PNAS USA</i> , 90:6796-6800 (1993).	
	105	Brown, et al., Evaluation of Cathepsins D and G and EC 3.4.24.15 as Candidate β -Secretase Proteases Using Peptide and Amyloid Precursor Protein Substrates, <i>Journal of Neurochemistry</i> , 66: 2436-2445 (1996).	
	106	Chevallier, et al., Cathepsin D displays in vitro β -secretase-like specificity, <i>Brain Research</i> , 750:11-19 (1997).	
	64	Chyung, et al. Novel β -Secretase Cleavage of β -Amyloid Precursor Protein in the Endoplasmic Reticulum/Intermediate Compartment of NT2N Cells, <i>Journal of Cell Biology</i> , 138: 671-680 (August 11, 1997).	
	107	Diedrich, et al., Nucleotide sequence of a cDNA encoding mouse cathepsin D, <i>Nucleic Acids Research</i> , 18:7184 (1990).	
	65	Elan Corporation, plc and Pharmacia Corporation announce research collaboration, News 08/09/2000, www.elancorp.com.	
	66	Evin, et al., Alzheimer's disease amyloid precursor protein (β APP): proteolytic processing, secretases and β A4 amyloid production, <i>Amyloid; Int. J. Exp. Clin. Invest.</i> 1: 263-280 (September 8, 1994).	
	67	Haass, et al., Amyloid β -peptide is Produced by Cultured Cells During Normal Metabolism, <i>Nature</i> , 359: 322-325 (September 24, 1992).	
	68	Haass, et al., The Swedish Mutation Causes Early-Onset Alzheimer's Disease by β -Secretase Cleavage Within the Secretory Pathway, <i>Nature Medicine</i> , 12: 1291-1296 (December 1995).	
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	70	Hirosawa, et al., Characterization of cDNA Clones Selected by the GeneMark Analysis from Size-Fractionated cDNA Libraries From Human Brain, <i>DNA Res.</i> , 6(5): 329-336 (October 29, 1999).	

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	71	Hussain, et al., Identification of a Novel Aspartic Protease (Asp 2) as β -Secretase, <i>Molecular and Cellular Neuroscience</i> , 14: 419-427 (1999).	
	72	Kang, et al., The Precursor of Alzheimer's Disease Amyloid A4 Protein Resembles a Cell-Surface Receptor, <i>Nature</i> , 325: 733-736 (February 19, 1987).	
	73	Kitaguchi, et al., Novel Precursor of Alzheimer's Disease Amyloid Protein Shows Protease Inhibitory Activity, <i>Nature</i> , 331: 530-532 (February 11, 1988).	
	74	Knops, et al., Cell-type and Amyloid Precursor Protein-type Specific Inhibition of $A\beta$ Release by Bafilomycin A1, a Selective Inhibitor of Vacuolar ATPases, <i>Journal of Biological Chemistry</i> , 270: 2419-2422 (February 10, 1995).	
	75	Koo and Squazzo, Evidence that Production and Release of Amyloid β -Protein Involves the Endocytic Pathway, <i>Journal of Biological Chemistry</i> , 269: 17386-17389 (July 1, 1994).	
	108	Majer, et al., Structure-based subsite specificity mapping of human cathepsin D using statine-based inhibitors, <i>Protein Science</i> , 6:1458-1466 (1997).	
	76	Mullan, et al., A Pathogenic Mutation for Probable Alzheimer's Disease in the APP Gene at the N-Terminus of β -Amyloid, <i>Nature Genetics</i> 1: 345-347, (August 1992).	
	77	PCT Search report for PCT/US99/20881	
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	79	Ponte, et al., A New A4 Amyloid mRNA Contains a Domain Homologous to Serine Proteinase Inhibitors, <i>Nature</i> , 331: 525-527 (February 11, 1988).	
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	110	Schechter, et al., On the size of the active site in proteases. I. Papain, <i>Biochemical and Biophysical Research Communications</i> , 27:157-162 (1967).	

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	80	Seubert, et al. Secretion of β -amyloid Precursor Protein Cleaved at the Amino Terminus of the β -amyloid Peptide, <i>Nature</i> , 361: 260-263 (January 21, 1993).	
	81	Sinha, et al., Purification and Cloning of Amyloid Precursor Protein β -Secretase from Human Brain, <i>Nature</i> , 402: 537-540 (December, 2 1999).	
	82	Szecs, The Aspartic Proteases, <i>Scand. J. Clin. Lab. Invest.</i> , 52 (suppl. 210): 5-22 (1992).	
	83	Tanzi, et al., Protease Inhibitor Domain Encoded by an Amyloid Protein Precursor mRNA Associated with Alzheimer's Disease, <i>Nature</i> , 331: 528-530 (February 11, 1988).	
	93	Thompson, et al., Expression and characterization of human β -secretase candidates metalloendopeptidase MP78 and cathepsin D in β APP-overexpressing cells, <i>Molecular Brain Research</i> , 48:206-214.	
	84	Vasser, et al., β -secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE, <i>Science</i> , 286 (5440): 735-41 (October 22, 1999).	
	85	Yan, et al., Membrane-anchored Aspartyl Protease with Alzheimer's Disease β -Secretase Activity, <i>Nature</i> , 402: 533-537 (December 2, 1999).	
	101	Young, et al., HIV-1 Protease Inhibitors Based on Hydroxyethylene Dipeptide Isosteres: An Investigation into the Role of the P ₁ Side Chain on Structure-Activity, <i>J. Med. Chem.</i> , 35:1702-1709 (1992).	
	86	Zhao, et al., β -Secretase Processing of the β -Amyloid Precursor Protein in Transgenic Mice Is Efficient in Neurons but Inefficient in Astrocytes, <i>Journal of Biological Chemistry</i> , 271: 31407-31411 (December 6, 1996).	

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